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TITLE: Methods and kits for indirect labeling of nucleic acids

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CLAIMS:

What is claimed is:

1. A method for producing a detectably labeled nucleic acid, said method comprising: enzymatically generating by template dependent polymerization an oligonucleotide tagged nucleic acid, wherein said oligonucleotide tagged nucleic acid comprises an oligonucleotide tag; and contacting said oligonucleotide tagged nucleic acid with a labeled oligonucleotide complementary to said oligonucleotide tag under conditions sufficient for said labeled oligonucleotide to hybridize to said oligonucleotide tag; whereby a detectably labeled nucleic acid is produced.

2. The method according to claim 1, wherein said detectably labeled nucleic acid is directly detectable.

3. The method according to claim 2, wherein said directly detectable label is fluorescent.

4. A method for producing a detectably labeled population of target nucleic acids from an initial nucleic acid sample, said method comprising: enzymatically generating a population of oligonucleotide tagged target nucleic acids from an initial nucleic acid sample, wherein said oligonucleotide tagged target nucleic acids in said population comprise the same oligonucleotide tag; and contacting said population of oligonucleotide tagged target nucleic acids with labeled oligonucleotides complementary to said oligonucleotide tag of each oligonucleotide tagged target nucleic acid under hybridization conditions; whereby a detectably labeled population of target nucleic acids is produced.

5. The method according to claim 4, wherein said nucleic acid sample is an mRNA sample.

6. The method according to claim 5, wherein a primer that comprises an oligo dT domain and said oligonucleotide tag is employed in said enzymatically generating step.

7. The method according to claim 6, wherein said primer further comprises an RNA polymerase promoter domain.

8. The method according to claim 6, wherein said population of detectably labeled target nucleic acids is labeled with a fluorescent label.

9. A method of detecting the presence of a nucleic acid analyte in a target sample, said method comprising: (a) enzymatically generating an oligonucleotide tagged target nucleic acid from said nucleic acid analyte, wherein said oligonucleotide tagged target nucleic acid comprises an oligonucleotide tag; and (b) producing a hybridized complex that comprises: (i) said tagged target nucleic acid; (ii) an oligonucleotide label; and (iii) a probe nucleic acid; (c) detecting the presence of said hybridized complex; and (d) relating the presence of said hybridized complex to the presence of said nucleic acid analyte in said sample; whereby the presence of said nucleic acid analyte in said sample is detected.

10. The method according to claim 9, wherein said probe is stably associated with the surface of a solid support.

11. The method according to claim 9, wherein said probe is present on an array.

12. The method according to claim 9, wherein said labeled oligonucleotide is fluorescently labeled.

13. The method according to claim 9, wherein a primer comprising an oligo dT region and said oligonucleotide tag is employed in said enzymatically generating step.

14. The method according to claim 13, wherein said primer further comprises an RNA polymerase promoter.

15. The method according to claim 9, wherein said method further comprises transmitting data obtained from at least one of said detecting and related steps to a remote location.

16. A method for obtaining an expression profile for at least a representative number of genes in a cell, said method comprising: (a) enzymatically generating a population of oligonucleotide tagged nucleic acids from an mRNA sample derived from said cell, wherein each oligonucleotide tagged nucleic acid comprises an oligonucleotide tag; (b) producing at least one hybridized complex comprising: (i) a tagged target nucleic acid; (ii) a labeled oligonucleotide; and (iii) a probe nucleic acid stably associated with the surface of a solid support; (c) detecting the presence of said at least one hybridized complex on said array surface; and (d)

deriving an expression profile for said cell from said detected at least one hybridized complex; whereby said expression profile for at least a representative number of genes in said cell is obtained.

17. The method according to claim 16, wherein a primer comprising an oligo dT domain and said oligonucleotide tag is employed in said enzymatically generating step.

18. The method according to claim 17, wherein said primer further comprises an RNA polymerase promoter.

19. The method according to claim 16, wherein said labeled oligonucleotide is fluorescently labeled.

20. The method according to claim 16, wherein said method further comprises transmitting data obtained from at least one of said detecting and deriving steps to a remote location.

21. A method for comparing the expression profiles of at least two distinct samples, said method comprising: (a) enzymatically generating: (i) a first population of oligonucleotide tagged nucleic acids from an mRNA sample derived from a first sample, wherein each oligonucleotide tagged nucleic acid of said first population comprises a first oligonucleotide tag; and (ii) a second population of oligonucleotide tagged nucleic acids from an mRNA sample derived from a second sample, wherein each oligonucleotide tagged nucleic acid of said second population comprises a second oligonucleotide tag that differs from said first oligonucleotide tag; (b) hybridizing said first and second populations of oligonucleotide tagged target nucleic acids to an array of probe nucleic acids stably associated with the surface of a solid support, wherein said hybridizing occurs in the presence of: (i) first labeled oligonucleotide complementary to said first oligonucleotide tag of said first population; and (ii) second labeled oligonucleotide complementary to said second oligonucleotide tag of said second population; whereby hybridized complexes comprising said oligonucleotide tagged target nucleic acids, probe nucleic acids and labeled oligonucleotides are produced on the surface of said array; (c) detecting the presence of said hybridized complexes on said array surface; (d) deriving an expression profile for each of said cells from said detected hybridized complexes; and (e) comparing the derived expression profiles of each of said cells; whereby the expression profiles of said at least two distinct cells are compared.

22. The method according to claim 21, wherein said first and second labels are distinguishable.

23. The method according to claim 22, wherein said first and second labels are fluorescent.

24. The method according to claim 21, wherein a primer comprising an oligo dT domain and said oligonucleotide tag is employed in said enzymatically generating step.

25. The method according to claim 24, wherein said primer further comprises an RNA polymerase promoter.

26. A kit for use in obtaining an expression profile for at least a representative number of genes in a cell, said kit comprising: (a) a first primer comprising an hybridization domain and an oligonucleotide tag; and (b) a first labeled oligonucleotide complementary to said oligonucleotide tag.

27. The kit according to claim 26, wherein said primer further comprises an RNA polymerase promoter.

28. The kit according to claim 26, wherein said hybridization domain is an oligo dT domain.

29. The kit according to claim 26, wherein said hybridization domain is a domain of random sequence.

30. The kit according to claim 26, wherein said kit further comprises an array of probe nucleic acids stably associated with the surface of a solid support.

31. The kit according to claim 26, wherein said kit further comprises: (a) a second primer comprising an hybridization domain and a second oligonucleotide tag having a sequence different from said first oligonucleotide tag; and (b) a second labeled oligonucleotide, wherein the label of said second labeled oligonucleotide is distinguishable from the label of said first labeled oligonucleotide.

32. The kit according to claim 29, wherein said second primer further comprises an RNA polymerase promoter.

33. The kit according to claim 26, wherein said kit further comprises an RNA polymerase.

34. The kit according to claim 26, wherein said first labeled oligonucleotide is labeled with a fluorescent label.

35. The kit according to claim 26, wherein said kit further comprises a computer readable storage medium on which is recorded an algorithm for designing oligonucleotide tag sequences.